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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/517,784 | 12/13/2004 | Gideon Gross | GROSS32 | 4624 |

1444 7590 11/12/2009

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| EXAMINER | |
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| ART UNIT | PAPER NUMBER |
|---|---|
| 1643 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 11/12/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/517,784 | GROSS ET AL. | |
| | Examiner | Art Unit | |
| | BRADLEY DUFFY | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *15 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1, 3, 5, 11-44, 47-53 and 58-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,11-44,47-53,58 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/12/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. The amendment filed April 15, 2009, is acknowledged and has been entered.

The Office has vacated the previously mailed notice of non-compliant amendments, some of which detail amendments that were not in compliance with 37 CFR 1.121. Despite this fact, it is apparent that the requirements to comply with 37 CFR 1.121 for the amendment filed April 15, 2009, and the previous amendments, have been waived. Nonetheless, Applicant is advised that all future amendments should be compliant with the rules set forth under 37 CFR 1.121; and for clarity, all future amendments to the specification and/or the claims should be made relative to the amendment filed April 15, 2009, so as to comply with the rules.

2. The declaration under 37 C.F.R. § 1.132 by Gideon Gross filed April 15, 2009, is acknowledged and has been entered.

3. Claims 1, 3, 5, 11-44, 47-53 and 58-59 are pending in the application and are under examination.

### *Response to the Declaration under 37 C.F.R. § 1.132*

4. The declaration under 37 C.F.R. § 1.132 by Gideon Gross filed April 15, 2009, details two experiments from Margalit et al (J. Immun., 176:217-224, 2006), a reference which was considered by the Examiner in the previous office action. A response to Applicant's arguments pertaining to the Margalit et al reference is set forth below.

### *Information Disclosure Statement*

5. The references cited in the information disclosure statement filed on September 12, 2007, have been considered.

***Specification***

6. The disclosure is objected to because of the following informalities:

a. The objection to the specification, because the use of improperly demarcated trademarks, is maintained. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Although it appears that Applicant has made a *bona fide* attempt to resolve this issue by appropriately amending the specification, additional examples an improperly demarcated trademarks appearing in the specification are noted, namely FACSCalibur™ and Easyject® (see, e.g., page 33).

Again, appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at <http://www.uspto.gov/web/menu/search.html>

b. The objection to the specification because of disclosures by the impermissible referral to embedded hyperlinks and/or other forms of browser-executable code, and to the Internet contents so identified, is maintained. Reference to hyperlinks and/or other forms of browser-executable code, and thus to the Internet contents so identified, is impermissible and therefore requires deletion.

In replying to the preceding amendment, Applicant amended the specification to delete "http://" from the disclosure at page 118, beginning in line 8; however, the specification still contains a link, namely "www.cancerimmunity.org/peptidedatabase/Tcellepitopes.htm". Even if the link were "inactivated", the disclosure still refers to the website, and to the Internet contents so identified.

Again, the attempt to incorporate essential or non-essential subject matter into the patent application by reference to a hyperlink and/or other forms of browser-

executable code, for example, (i.e., any reference to the contents of an Internet website) is considered to be an improper incorporation by reference and requires deletion.

By way of further explanation, MPEP 608.01(p) does not provide for incorporation of essential or non-essential material by reference to, for example, hyperlinks or other forms of browser-executable code. Essential subject matter may *only* be incorporated by reference to (1) US patents and pending US applications, or patents or other publications published by a foreign country or a regional patent office, (2) non-patent publications, (3) a US patent or application which itself incorporates material by reference, or (4) a foreign application. Non-essential information may *only* be incorporated by reference to (1) patents or applications published by the United States, or patents or other publications published by a foreign country or a regional patent office, (2) prior filed, commonly owned US applications, (3) non-patent publications. Not provided for by MPEP 608.01(p) is the inclusion of material in an application by reference to a website and its contents.

It is impermissible that a patent's disclosure incorporate essential or non-essential material by reference to, for example, embedded hyperlinks and/or other forms of browser-executable code and to the Internet contents so identified, because the information contained in the websites or databases to which the hyperlinks or other forms of browser-executable code connect may not be maintained on the Internet for the duration of the patent's term and may not contain the same information after the filing date of an application that was contained in the website or database on or before the filing date of the application. Since the information contained in a website may vary, it is not evident that information contained in a website will always remain useful the practitioner or even applicable to the invention; and information contained in an extinct website cannot possibly be helpful to the practitioner. Furthermore, the validity of a patent containing a reference to a hyperlink or other form of browser-executable code may be reasonably questioned if the website(s) to which the hyperlink(s) connect were relied upon by the patentee(s) to provide sufficient disclosure or description of the invention to meet the requirements of 35 USC § 112, first and second paragraphs. As such, recitation of such references is not permitted.

In further accordance with M.P.E.P. § 608.01(VII), a hyperlink or other form of browser-executable code may be permitted if the hyperlink or other form of browser-executable code is part of the claimed invention, and in such a case, the Office would disable the hyperlink or other form of browser-executable code; but the hyperlink originally disclosed in this application is not part of the invention. Rather the hyperlink was intended to provide inclusion of information by reference to the website so identified; therefore, Applicant is again reminded that the attempt to incorporate subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code, or to the Internet contents so identified, is considered to be an improper incorporation by reference. Other material ("Nonessential material") may only be incorporated by reference to U.S. patents, U.S. patent application publications, foreign patents, foreign published applications, prior and concurrently filed commonly owned U.S. applications, or non-patent publications. See 37 C.F.R. § 1.57(d).

In general, if the Applicant expects to rely upon the information contained in the websites or databases referred to by such disclosures to satisfy the requirements set forth under 35 U.S.C. § 112, first paragraph, or to provide antecedent basis for the subject matter of claims in the instant application or related applications, and if the material is properly incorporated by reference in the referencing application, Applicant would be required to amend the specification of the referencing application to include the material incorporated by reference to the hyperlink or other forms of browser-executable web, or other non-permissible sources and to provide a declaration by Applicant or Applicant's representative stating that the amendatory material consists of the same material incorporated by reference in this application. See MPEP § 608.01(p).

If Applicant intends that information contained at the websites to which the disclosures refer be incorporated, Applicant is required to amend the specification to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by Applicant, or a practitioner representing Applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See In re Hawkins, 486 F.2d

569, 179 USPQ 157 (CCPA 1973); In re Hawkins, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and In re Hawkins, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Accordingly, it is maintained that the reference to the Cancer Immunity website to describe TAA peptides, is considered to be an improper incorporation by reference and is not permitted. See 37 CFR 1.57(d) and MPEP § 608.01(p).

Appropriate correction is required.

***Claim Objections***

7. Claims 1, 3, 5, 11-44, 47-53 and 58-59 are objected as being directed to inventions, which were not encompassed by the originally presented claims.

In this case, the originally presented claims were directed to a polynucleotide encoding a polypeptide, which comprises, in part, at least one antigenic peptide comprising an MHC class I epitope, wherein said *antigenic peptide is not related to an autoimmune disease*. Therefore, while the original claims limited the antigenic peptides to ones *not related to an autoimmune disease*, the claims, as presently amended, are directed to additional subject matter not before claimed or presented for prosecution on the merits, as for reasons before pointed out in Office actions mailed April 9, 2008, and July 7, 2009, (each of which has been now vacated by the Office). Moreover, the amendments filed after the first Office action on the merits have stricken the limitation, "not related to an autoimmune disease", such that the claimed invention encompasses *any* antigenic peptides, and not just those peptides which are "not related to an autoimmune disease".

As such, claims 1, 3, 5, 11-44, 47-53 and 58-59 are objected as being directed to inventions, which were not encompassed by the originally presented claims; and therefore, for search purposes the claims have been examined only to the extent that the claims read on the originally presented invention, i.e., wherein said antigenic peptides are *not related to an autoimmune disease*.

***Claim Rejections - 35 USC § 112***

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1, 3, 5, 11-44, 47-53 and 58-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1, 3, 5, 11-44, 47-53 and 58-59 are indefinite because the claims have been amended to recite an antigenic peptide comprising an MHC class I epitope, selected from the group consisting of a tumor-associated antigen (TAA), an antigen from a pathogen selected from the group consisting of a bacterial antigen, a viral antigen, a fungal antigen and a parasite antigen, and at least one idiotypic peptide expressed by autoreactive T lymphocytes". This renders the claims indefinite because it is unclear whether the *peptide* or the *epitope* is selected from the group consisting of a tumor-associated antigen (TAA), bacterial antigen, a viral antigen, a fungal antigen and a parasite antigen, and at least one idiotypic peptide expressed by autoreactive T lymphocytes. In this case, the claim previously recited a wherein clause that limited the antigenic peptide, and by removing the wherein clause the claims cannot be unambiguously construed. Accordingly, because the claims cannot be unambiguously construed it is, it is submitted that the metes and bounds of the subject matter that is regarded as the invention is not delineated with the clarity and particularity to satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph, so as permit the skilled artisan to know or determine infringing subject matter.

(b) The claims are also indefinite because the claims have been amended to recite "consisting of the full or partial transmembrane and/or cytoplasmic domain of a molecule selected from the group consisting of the human CD3 ζ polypeptide, CD40 and the MHC I class heavy chain of HLA-A, HLA-B or HLA-C molecule" which occurs after a comma. In this case, because the phrase occurs after a comma it is unclear what part of the claim the "consisting of" phrase is intended to modify. For this reason as well the claims cannot be unambiguously construed. Accordingly it is submitted that

the metes and bounds of the subject matter that is regarded as the invention is not delineated with the clarity and particularity to satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph, so as permit the skilled artisan to know or determine infringing subject matter.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1, 3, 5, 11-44, 47-53 and 58-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a NEW MATTER rejection.

In this case, the claims have been amended to remove the limitation that the antigenic peptide encoded by the polynucleotide "is not related to an autoimmune disease" (see e.g., claim 1).

Applicant has not indicated where support occurs in the specification for this amendment.

Notably, M.P.E.P. § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims". See M.P.E.P. § 714.02 and § 2163.06.

Nevertheless, as M.P.E.P. § 2163 further states: "The examiner has the initial burden of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the original disclosure a description of the invention defined by the claims. See *Wertheim*, 541 F.2d at 263, 191 USPQ at 97".

After reviewing the specification, it does not appear that the specification, including the claims, as originally filed, provides adequate support for the language of

the amended claims, which are directed to any peptide, and not just to those peptides, which are not related to an autoimmune disease.

The abstract of the specification, for example, makes clear that the invention is considered to involve only those peptides that are not related to an autoimmune disease, and not just any peptide.

More particularly, it is noted that the abstract characterizes the invention as follows (emboldening added for emphasis):

> The invention provides a polynucleotide comprising a sequence encoding a polypeptide comprising a beta2-microglobulin molecule linked through its carboxyl terminal to a polypeptide stretch that allows the anchorage of the beta2-microglobulin molecule to the cell membrane, and through its amino terminal to at least one antigenic peptide comprising a MHC class I epitope, **wherein said antigenic peptide is not related to an autoimmune disease and is preferably derived from a tumor-associated antigen or from a pathogenic antigen**. Antigen presenting cells, and DNA and cellular vaccines for treatment of cancer and infectious diseases, are also provided.

Not at all inconsistently, the very first paragraph describing the Filed of the Invention clearly sets forth that the invention involves peptides, which are *not* related to an autoimmune disease (again with emboldening added for emphasis):

> The present invention is in the field of Immunology and relates to DNA molecules encoding chimeric polypeptides comprising β-microglobulin and a polypeptide stretch for anchoring the β2-microglobulin molecule to the cell membrane, herein referred to as single-chimeric β-microglobulin (scβ2m), and to such DNA molecules further comprising at least one antigenic peptide linked to the amino terminal of the 132-microglobulin molecule, herein referred to as double-chimeric β-microglobulin (dcβ2m), **wherein the antigenic peptide is not a peptide related to an autoimmune disease**, and to antigen-presenting ceils expressing said scβ2m and dcβ2m polypeptides, as novel tools for efficient CTL induction for the treatment of cancer and infectious diseases.

Then, too, originally presented claim 1 clearly sets forth that the invention involves a peptide that is *not* related to an autoimmune disease:

> A polynucleotide comprising a sequence encoding a polypeptide that is capable of high level presentation of antigenic peptides on antigen-presenting cells, wherein the polypeptide comprises a 132-microglobulin molecule that is linked through its carboxyl terminal to a polypeptide stretch that allows the anchorage of the 13z-microglobulin molecule to the cell membrane, and through its amino terminal to at least one antigenic peptide comprising a MHC class I epitope, **wherein said antigenic peptide is not related to an autoimmune disease**. [1]

[1] Emphasis added

Nowhere in the specification is there any disclosure, which characterizes the peptide as a peptide that is related to an autoimmune disease. Always the peptide is described as a peptide that is not related to an autoimmune disease.

Accordingly, it is submitted that the key disclosures noted above point to the fact that the invention originally contemplated by Applicant involved peptides, which are *not* related to an autoimmune disease – and by absence of supporting disclosure, it is apparent that Applicant did not contemplate the invention, now claimed, which involves the use of any of the claimed peptides, none of which are not necessarily those to which the originally presented claims were directed, as none are necessarily not related to an autoimmune disease.

It is therefore evident that the amendment to the claims, which has stricken the limitation, "not related to an autoimmune disease" has violated the written description requirement set forth under 35 U.S.C. §112, first paragraph, by introducing new concepts, which were not adequately embraced by the disclosure or the claims, as originally filed or presented for prosecution on the merits.

Turning to a second issue, now, it is further noted that the claims have been amended to add the limitation, "the full or partial transmembrane and/or cytoplasmic domain of … the human CD3 ζ polypeptide"

Here again, Applicant has not indicated where written support for such changes in the language of the claims occurs in the specification, including the claims, as originally filed.

After reviewing the specification, it does not appear that the specification, including the claims, as originally filed, provides adequate support for the language of the amended claims.

For example, at page 13 the specification sets forth that:

> In a preferred embodiment, the anchoring residue of the chimeric molecule comprises **the transmembranal and cytoplasmic regions of the human T-cell receptor CD3 ζ polypeptid**e, a signal transduction element capable of activating T cells.[2]

Furthermore while original claim 8 supports the limitation, "the transmembranal

and cytoplasmic regions of the human CD3 ζ polypeptide", support for "*the partial transmembrane and/or cytoplasmic domain* of the human CD3 ζ polypeptide" could not be found in the specification, as filed.

Accordingly, it is submitted that this new limitation, which does not appear to be supported in the specification as filed, has in fact introduced new concepts, thereby violating the written description requirement set forth under 35 U.S.C. §112, first paragraph.

To remedy these, issues Applicant should amend the claims to cancel the new matter added by amendment.

13. The rejection of claims 1, 3, 5, 11-44, 47-53 and 58-59 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "written description" rejection.

Starting at page 20 of the amendment filed April 15, 2009, Applicant has traversed the propriety of this ground of rejection.

Applicant's arguments have been carefully considered but are not found persuasive for the following reasons:

Again, the considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, ``Written Description" Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001; hereafter "Guidelines"). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

In this case, Applicant appears to argue that the claims as amended which are

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[2] Emphasis added

drawn to polynucleotides encoding, in part, "antigenic peptides comprising an MHC class I epitope" and/or "the full or ***partial*** transmembrane and/or cytoplasmic domain of a molecule selected from the group consisting of the human CD3 ζ polypeptide, CD40 and the MHC I class heavy chain of HLA-A, HLA-B or HLA-C molecule are adequately described because one of skill in the art would be able to envision transmembrane polypeptides with a cytoplasmic tail that have the function of anchoring the polypeptide to the cell membrane. Applicant further submits that new claims 58 and 59 correspond to the scope considered to be adequately described by the Examiner.

In response, the claims still recite any ***"partial*** transmembrane and/or cytoplasmic domain" selected from the human CD3 ζ polypeptide, CD40 and the MHC I class heavy chain of HLA-A, HLA-B or HLA-C molecule and the previous office action did not indicate that such ***"partial*** transmembrane and/or cytoplasmic domains" had been adequately described as having the requisite anchoring function because the rejection set forth that the specification adequately described that the transmembrane and cytoplasmic domains from the MHC class I heavy chain of HLA-A2 or from the human CD3 ζ polypeptide had the requisite anchoring function. In this case, the specification does not identify ***partial*** transmembrane domains or ***partial*** cytoplasmic domains of a human CD3 ζ polypeptide, CD40 or the MHC I class heavy chain of HLA-A, HLA-B or HLA-C molecules that would be sufficient to retain the requisite anchoring function, so it is maintained that the claimed invention is not adequately described. Accordingly, new claims 58 and 59 do not correspond to the scope considered to be adequately described by the Examiner since they refer to ***partial*** transmembrane domains and/or ***partial*** cytoplasmic domains.

Secondly, the previous office action set forth that the specification only "adequately describes antigenic peptides comprising a MHC class I epitope, wherein the peptide has a defined amino acid sequence in the specification (see for example pages 15-17 that discloses SEQ ID NOS giving the amino acid sequence of known MHC class I epitopes)" and Applicant has not provided any direct arguments that traverse this part of the rejection. Accordingly, this part rejection is being maintained for

the claims that encompass antigenic peptides comprising a MHC class I epitope other than those particularly identified by amino acid sequence in the specification.

Finally, it is noted that the claims also appear to lack adequate written description for the reasons set forth in the above NEW MATTER rejection.

Accordingly, after careful and complete consideration of Applicant's arguments, for these reasons and as explained more fully in the previous Office action, the specification as filed would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed and this rejection is maintained.

14. The rejection of claims 1, 3, 5, 11-44, 47-53 and 58-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

MPEP § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Starting at page 22 of the amendment filed April 15, 2009, Applicant has traversed the propriety of this ground of rejection.

Applicant's arguments have been carefully considered but are not found persuasive for the following reasons:

In this case, Applicant appears to argue that the claimed inventions are enabled because vaccines have been used for hundreds of years to prevent diseases and that preventing diseases is what is being claimed, not preventing infections. Applicant further argues that the Examiner has cited attempts in the past that have failed to create

vaccines that generate antigen specific CTLs to treat or prevent diseases or cancer and Applicant has further presented two experiments conducted in a mouse xenograft tumor model wherein melanoma tumors were inhibited by immunization with an irradiated lymphoma cell line expressing a polynucleotide of the invention.

In response, as a first point, it is noted that Applicant has not provided any direct arguments pertaining to the ability of the skilled artisan to make polynucleotides commensurate in scope with the claimed polynucleotides. Accordingly, as set froth in the previous action is maintained that, insofar as the products and methods are drawn to polynucleotides that one of skill in the art would not be able to immediately envision as set forth in the above rejection of the claims as lacking adequate written description rejection, one of skill in the art would be subject to undue experimentation to make polynucleotides commensurate in scope with the claimed invention. In this case, the specification lacks any specific non-general guidance on how to predict which partial transmembrane or partial cytoplasmic domains will have the required anchoring function and how to predict which peptides are antigenic MHC class I epitopes.

Secondly with respect to Applicant's argument the claims are drawn to preventing diseases which has been accomplished by vaccines for hundreds of years, the examiner acknowledges that other vaccines are known, but what is being claimed is are vaccines for preventing or treating cancer (see e.g., claim 38) or DNA vaccines or vaccines comprising antigen preventing cells for preventing or treating a disease caused by a pathogenic organism, wherein the pathogen is a bacteria, virus, fungus or parasite (see e.g., claims 39 and 40) which are not equivalent to the vaccines which have been used for hundreds of years. Furthermore, since bacteria, viruses, fungi and parasites infect hosts and cause infection, the claims reasonably encompass vaccines for preventing infections which for the reasons set forth in the previous office action are not enabled. Additionally, with respect to the prevention of cancer, since Applicant has not presented any direct arguments directed to the prevention of cancer it is maintained that one of skill in the art would be subject to undue and unreasonable experimentation to use the claimed vaccines to prevent cancer.

Finally to address Applicant's argument pertaining to the evidence of attempts

that have failed to create vaccines that generate antigen specific CTLs to treat diseases or cancer in the past, the Examiner set forth this evidence to establish the unpredictability in the art pertaining to using such vaccines to treat diseases or cancer. Notably, while Applicant's argument points to the declaration of Gideon Gross which sets forth two experiments conducted in a mouse xenograft tumor model wherein melanoma tumors were inhibited by immunization with an irradiated lymphoma cell line expressing a polynucleotide encompassed by the invention and which were part of the Margalit et al reference (J. Immun., 176:217-224, 2006) that was previously considered by the Examiner, none of the instant claims are drawn to irradiated cells expressing a polynucleotide of the invention or to methods of treating subjects by administering such irradiated cells. In this case, no evidence has been presented which is reasonably commensurate with the scope of the claimed invention that established that one of skill in the art could use the full scope claimed polynucleotides, vaccines and methods of immunizing mammal without undue and unreasonable experimentation.

Applicant is reminded that reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

Applicant further appears to argue that the art is not unpredictable because while Margalit et al (J. Immun., 176:217-224, 2006) teach injecting a mouse model with a vaccine comprising cells presenting a polypeptide comprising β2-microglubilin linked to the h-2K anchor and the MHC class I epitope comprising amino acids 181-188 TRP-2 which is encoded by a polynucleotide encompassed by the claims and that this vaccine *fails* to suppress the growth of established tumors (see entire document, e.g., page 219, figure 1 and page 222, left column), the Examiner has missed the authors explanation of this phenomenon, namely that the initial administration of M05 cells (a spontaneous murine BI6 melanoma) in a non-immunostimulatory context may have enhanced the activity of regulatory T cells (Tregs) to a level that prevented later induction of TRP-2-specific CTLs by the transformed antigen presenting cells expressing the polypeptide of the invention.

In response, the Examiner considered the teachings of Margalit et al (J. Immun., 176:217-224, 2006) as a whole. Notably, Margalit et al specifically states that “they

have not investigated this phenomenon further" at page 222. Accordingly, while Margalit et al hypothesizes on factors that could have caused the phenomenon, there is no evidence to support their hypothesis. Therefore, is maintained that Margalit et al taken as a whole evidences the unpredictability in the art.

Finally, Applicant further appears to argue that the art is not unpredictable because "Applicants would like to draw the examiner's attention to the fact that a method causing very efficient killing of the tumor cells would leave no time for a natural selection process to take place".

In response, it is unclear how efficient killing of the tumor cells would need to be to leave no time for a natural selection process to take place which allows a cancer to evade the immune system and there does not appear to be any evidence of record that Applicant's claimed methods or vaccines leave no time for a natural selection process which allows the cancer evades the immune system as explained by Bodey et al. Therefore, is maintained that the teachings of Bodey et al taken as a whole evidences the unpredictability in the art.

In conclusion, upon careful and full consideration of Applicant's arguments and the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enabled the skilled artisan to make and/or use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation, and this rejection is being maintained.

## ***Conclusion***

15. No claim is allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR

1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Gross et al (WO 01/91698, 2001) teach polynucleotides that encode polypeptides comprising a β2-microglobulin polypeptide linked through its carboxy terminus to polypeptide stretch that allow the anchorage of β2-microglobulin to the cell membrane and through its amino terminus to at least one antigenic peptide comprising a MHC class I epitope, wherein said antigenic peptide is related to an autoimmune disease.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935. The examiner can normally be reached at Monday through Friday from 7:00 AM to 4:30 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Brad Duffy/
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Primary Examiner, Art Unit 1643

bd
November 6, 2009